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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,877	09/19/2001	Said I.A. Shalaby	AP32738; 066876.0103	9851

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EXAMINER
PATTEN, PATRICIA A

ART UNIT	PAPER NUMBER
1654	8

DATE MAILED: 07/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,877	SHALABY ET AL.	
	Examiner	Art Unit	
	Patricia A Patten	1654	

-- The MAILING DATE f this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 24-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VIIII in Paper No. 7 is acknowledged. The traversal is on the ground(s) that Groups X and XI are 'not sufficiently independent and distinct so as to require restriction in the present case' since these groups are all drawn to treating a viral infection comprising administration of *S.aegypiaca*. This is not found persuasive because as indicated in the Restriction Requirement of Paper No. 5, these claims are unrelated. The reason they are unrelated is because the method can be carried out with a materially different product as evidenced by the claims themselves. Further, the method according to Group X adds two unknown herbal ingredients. This is clearly a different composition than is claimed in Group VIIII.

As further indicated, the claims are also properly restrictable because they are combination/subcombinations of each other (please see Restriction requirement).

It is noted that claims 31 and 32 are properly placed in Group XII since claim 31 is dependant upon claim 27 and claim 32 is dependant upon claim 31. Group XII should have read 'claims 19 and 27-32. This was an inadvertent error.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-33 are pending in the application. Claims 1-18 and 24-32 have been withdrawn from further consideration on the merits as being drawn to a non-elected invention.

Claims 19-23 were examined on the merits.

Specification

The disclosure is objected to because of the following informalities:

The Specification should properly begin with the title of the Invention. In the Instant case, Applicants have included the Attorney's name and address, along with the Inventor's name and address. Because this information is not needed directly in the disclosure, it is asked that Applicants delete this information. (i.e., beginning with 'Baker Botts' and ending with 'have invented' should be deleted. Further, it is noted that if this information is deleted, the phrase which states 'of which the following is a' should therefore also be deleted since leaving this phrase would result in an incomplete sentence.

Appropriate correction is required.

Claim Objections

Claim 21 is objected to because of the following informalities:

Claim 21 is missing a period at the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating hepatitis B or C virus by administration of either composition disclosed in Example 1 as actually displaying positive results, does not reasonably provide enablement for treating any virus with extracts from *S.aegyptiaca* and at least one other herb such as *C.proximus* for example. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The following will demonstrate that the claims are not enabled for their full scope. Specifically:

(1) The claims are not enabled for a method for treating any other viruses besides HBV and HCV .

(2) The claims are not enabled for treatment of HBV or HCV (or any other virus) with any *extracts* besides *E. elaterium*, because the Instant specification only demonstrated efficacy with regard to whole, ground plant matter and the juice of *E. elaterium*.

(3)The claims are not enabled for treatment of HBV or HCV (or any other virus) with any combination of herbs, but *are* enabled for the compositions/mixture of components which were administered to Groups A, C or D which actually displayed positive results.

(1)

In the Instant case, Applicants have not demonstrated in the Instant disclosure where other viruses such as HIV (which causes aids) or herpes simplex virus were treated with the compositions administered to the patients in the study group. Since the patients who participated in the study were not indicated as having HIV or herpes

simplex virus (HSV), it appears that there is not even a single example of where any of the compositions of the Instant invention were beneficial for treating HIV or HSV. Applicant describes the term 'treating' as 'at a minimum...inhibiting the progression of the viral infection which can be ascertained qualitatively (e.g., by a reduction in clinical symptoms) or quantitatively (e.g., by a reduction in viral load or other quantifiable criteria) (p. 17, Instant specification). It is noted that according to Applicants description of the term 'treating', the Instant specification fails to address these parameters with regard to any other viruses besides HBV and HCV.

Regarding HIV treatments, it is well known in the art that retroviral infections in general and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include; the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein, the fact that the modes of viral transmission include both virus-infected mononuclear cells which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission, the existence of a latent form of the virus, the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier, and the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation.

Because of the questionability of potential AIDS treatments, the most promising quantified assay to predict efficacy of a potential anti-AIDS drug is the *in-vivo* HIV viral load assay. A decrease in the HIV viral load would necessarily correspond to a 'treatment' of AIDS since it is the HIV virus itself which would need to diminish in order to substantiate an efficacious treatment for AIDS. It is not found in the Instant specification where the viral load of HIV or herpes has decreased upon *in-vivo* administration of any composition as described in the Instant specification.

With regard to the state of the art, the most promising quantified assay to predict efficacy of a potential anti-AIDS drug is the *in-vivo* HIV viral load assay: "Measuring viral load level is an important part of assessing a patient's disease prognosis and response to drug therapy..." (Blood Weekly 9/2002). "The US. Department of Health and Human Services and the Henry J. Kaiser Foundation, [6] as well as the International AIDS Society-USA Panel [,'] currently suggest that the results of PVL testing should be an essential parameter in decisions on initiating or changing antiretroviral drug therapy" (Mylonakis et al. American Family Physician, 2/2001).

Therefore, evidence of a decrease in the HIV viral load of an AIDS infected patient would necessarily correspond to a promising 'treatment' of AIDS since it is the HIV virus itself which would need to diminish in order to validate an efficacious treatment for AIDS. Because there is no evidence, or even suggestion within the

Instant specification that AIDS or herpes has actually been 'treated' by hindering or subduing the virility of the HIV or herpes, one of skill in the art would have trouble ascertaining how *to use the composition of the present invention commensurate in scope with the claimed invention* without actually performing tedious, time consuming clinical trials.

(2)

The Instant specification is not enabled for treating HBV or HCV with an extract of any of the plants besides *Ecballium elaterium*. Although the Instant specification teaches compositions comprising different combinations of plant extracts, it was the plants themselves which were found efficacious toward hepatitis. The Instant specification fails to teach how to make or use extracts of, for example, Formula 1 (Example 1) which would display positive results toward hepatitis.

The art of phytochemistry is unpredictable with regard to plant extracts. Plants, and parts thereof (i.e., fruits, stems, leaves, pollen, pistils, roots, rhizomes), are intricate living organisms which inherently possess an enormously diverse array of potential pharmacological ingredients. Just recently has the scientific community begun examining plants (as well as parts thereof) to evaluate their phytochemical constituents for medicinal purposes.

It is well known in the art that polarity of solvents plays a key role in determining the final product obtained by an extraction. However, because many phytochemicals remain undiscovered, the skilled artisan has to make his best educated guess as to what types of phytochemicals will be successfully extracted with a solvent of a particular polarity. Often times, unless the constituents in a particular plant extract have been well evaluated and documented in the literature, the skilled artisan must adhere to trial and error protocols in order to quantitatively determine phytochemical constituents present in samples obtained from respective extraction procedures. These procedures are common when, for example, a plant or part thereof has been documented in the literature as possessing some medicinal quality. The skilled artisan would need to perform numerous extraction protocols in attempt to isolate the particular ingredient which has this medicinal quality. Typically, *beginning* with the first crude extraction, ***it is a guess*** as to weather or not the extract will possess the inherent medicinal quality. Take for example, the grape, *Vitis vinefera*. If this fruit was documented in the literature as having a particular medicinal qualities, the skilled artisan may feel the need to extract and isolate the medicinally beneficial ingredient.

First, the skilled artisan would need to ascertain if the active ingredient is found on the inside of the fruit; i.e., pulp or juice, or if alternatively, the active ingredient was found in the skin of the fruit. Thus, a first 'extract' may be obtained via pressing the fruit to obtain the juice and pulp of the fruit. The pulp and juice of the fruit would constitute a first product ('extract') with many various cell constituents. Of course, a determination

would need to be made of if the extract, in this case, the pulp and the juice, actually possess the medicinal qualities as previously documented. If for example, the pulp and the juice of the grape did not prove to possess the documented medicinal quality, the skilled artisan would then test the skin of the grape for said quality (commonly, prior to solvent extraction, homogenization of the solids occurs via blending or vortexing). If the skin of the grape actually possessed the documented quality, the skilled artisan may then attempt to purify the ingredient further. Then, the skilled artisan will, by trial and error, attempt to perform step-wise extractions to isolate the active ingredient. If the first extraction attempt with a particular solvent fails, another solvent will be tried. Thus, beginning with the initial extraction, a first product is yielded which was extracted with the solvent, and a second product is yielded which remains because it did not possess a similar polarity to the solvent.

Unpredictability with regard to plant extracts has been well documented in the art. Revilla et al. for example (1998) showed that the slightest variations in polarity of solvent and reaction time upon grape extraction, provided respective products with unique characteristic properties (See Tables 1, 2, 4, 5, 6 and 7). In turn, each product would possess varying pharmacological properties based upon their respective phytochemical constituents. Each successive extraction yields different products due to the exclusion of ingredients based on the polarity of the solvents solvating constituents with similar polarities. Subsequently, the properties of each possible plethora of

different types of extracts from each plant material as Instantly recited would need to be evaluated for efficacy.

Additionally, according to the Stedman's dictionary 27th Ed, the term 'extract' means 'A concentrated preparation of a drug obtained by removing the active constituents of the drug with suitable solvents...'. Thus, purification of any of these products in the illustrative example to yield a specific phytochemical would constitute an 'extract' judging from the definition provided by Stedman's Medical Dictionary. Therefore, resveratrol, a phytochemical inherent in grapes, is deemed to be an 'extract' of grapes since it is obtained by the process outlined in Stedman's. Hence, each respective phytochemical found within grapes constitutes an extract once it is 'extracted' away from the rest of the grape's constituents as is each phytochemical 'extracted' from each of the Instantly recited plants.

The before mentioned is evidence that each respective product obtained from an extraction is unpredictable in nature. Even the most skilled of artisans would need to quantify each product for constituents as well as medicinal efficacy. In the Instant case, Applicants have not set forth any information or guidance to direct the skilled artisan to ascertain *where* in the plant matter the active ingredients are in the plants (i.e., water extract, distillation product, alcoholic extract, benzene extract etc.). Thus, to practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a

substantial inventive contribution on the part of a practitioner to ascertain what other extracts besides *Ecballium elaterium* would actually decrease HBV and HCV load and subsequently treat said viral infections. This inventive contribution would involve tedious trial and error protocols **without the expectation of success for the reasons set forth** *supra*.

(3)

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because treatment of viruses are relatively rare, and may be unbelievable in the absence of strong supporting evidence. As the state of the art stands, viruses are quite unpredictable in nature, and most viruses are difficult to treat. With regard to hepatitis C for example, Davis, G. reported in the British Medical Journal that "Chronic infection with the hepatitis C virus is extremely prevalent, averaging 1% to 2% of the world poplulation" (11/17/2001) (p.1). To date, as Davis explains, only a few viable treatments for Hepatitis C have emerged within the last two decades, namely, treatments with interferons (p.2). With regard to hepatitis B, Cancerweekly Plus reported "Although hepatitis B viral infections pose a serious health threat worldwide, few drugs are currently available to treat and ultimately prevent the progression of chronic disease," (quoting Professor Daniel Shouval, MD, Hadassah Medical Organization) "The

development of new, effective therapies has been hampered by the lack of a relevant small animal model for HBV that uses the human form of the hepatitis virus. At this point in time, there are a large number of potential therapeutic agents awaiting preclinical evaluation. The Trimera disease model circumvents many issues facing other animal models based on human HBV, including the staggering costs, small sample sizes, and difficulty in working with large animals."

Subsequently, in addition to the reasoning that the Instant claims are not enabled for a treatment of any virus with any extract of herb, it is deemed that the Instant claims are not enabled for every combination of herbs as recited in the Instant claims; i.e., *S. aegyptiaca* in combination with *C. proximus* for example (claim 19) for treating viruses such as HBV or HCV especially considering the tenacity of these viruses and the rarity of drugs which actually treat the viruses.

The Instant specification has shown that the combination of 12 ground herbs produced positive results with regard to hepatitis B and C disease parameters as indicated in Tables 4 and 5. Thus, Applicants are claiming that only two of the herbs as listed in claim 19 will manifest beneficial results with regard to HBV and HCV and yet the examples clearly indicate that in one example, a combination of 12 herbs were used, and in the other example the juice of *Ecballium elaterium* (which is an enabled embodiment). The specification is Lacking critical guidance that would indicate that the active ingredient which is efficacious toward HBV and HCV is specifically found in *S.*

aegyptiaca, and that *S. aegyptiaca,* in combination with any of the other listed herbs would perform effectively toward HBV and HCV. Therefore, no nexus between S. aegyptiaca and HBV and HCV has been demonstrated. Because of the lack of guidance in the Specification, the skilled artisan would need to perform undue experimentation to ascertain exactly what other combination of herbs as listed in claim 19 would actually work. This experimentation would not simply be routine; as Applicants indicate in the Instant specification, these studies were performed with human subjects over an extended period of time. Thus, this experimentation would be expensive and time consuming without any expectation of success.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases

involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Claims are free of the art. The closest prior art of record is Shawkat (US 5,648,089) who disclosed a method for treating hepatitis with a combination of nine herbs including *E. elaterium* and *N. Sativa* but did not teach the incorporation of *S. aegyptiaca*. *S. aegyptiaca* and/or extracts thereof were not found in the prior art for treating HBV or HCV or any other virus. Therefore, no motivation could be found to combine *S. aegyptiaca* extract with any of the other listed extracts to treat a viral infection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703)308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. The official After final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

July 16, 2003

Patricia Patten